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最終頁に続く

(54)【発明の名称】使い捨て滅菌済み流体レセプタクルサンプリング装置

(57)【要約】
【課題】使い捨ての廃棄性を推進するようその構造が十分に安価であり、流体レセプタクルにおいて一般的に見られる標準工業ポートにおいて使用することが可能であり、１回の滅菌周期および／または排気される前に幾つかの良好な滅菌された流体試料を抽出することを可能にする流体サンプリング装置を提供する。
【解決手段】本発明は、ポート挿入部と、複数の可撓性導管と、複数の試料用容器とを有する流体サンプリング装置を提供する。ポート挿入部は、複数のシャフトが中を通るボディ、および、流体が中を流れることを可能にする上記シャフトのいずれかを個別的に開閉する試料ゲート手段を含む。可撓性導管は、細長い部材と同じ数だけ設けられ、各可撓性導管は個々のシャフトに接続されるか流体連通される。試料用容器は、導管と同じ数だけ設けられ、各試料用容器はシャフトに接続される側とは反対側で個々の導管に接続される。
【選択図】図１

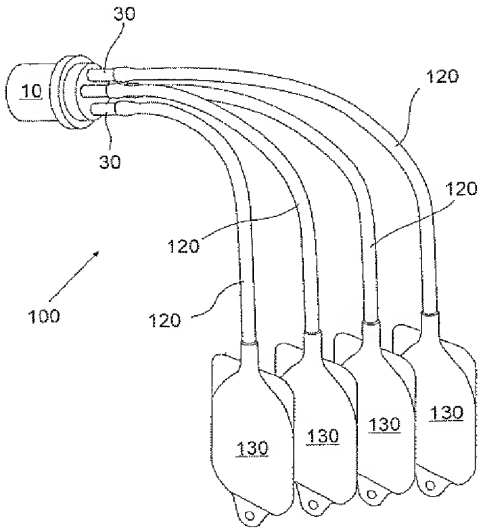

Figure 1

【特許請求の範囲】
【請求項1】
（ａ）複数のシャフトが中を通るボディ、および、流体の流れを可能にするよう前記シャフトのいずれかを個別的に開閉する試料ゲート手段を含み、前記試料ゲート手段が「開」位置と「閉」位置の間で移動可能な単一のまたは複数の部材を含み、流体は前記「開」位置では前記シャフトの一つを通って前記ボディを流れ、前記「閉」位置では流れない、ポート挿入部と、
（ｂ）個々のシャフトとそれぞれ流体連通する、前記複数のシャフトと同じ数の複数の可撓性導管と、
（ｃ）個々の導管とそれぞれ流体連通する、前記複数の導管と同じ数の複数の試料用容器とを有する、流体サンプリング装置。
【請求項2】
前記試料用容器は柔軟な袋である、請求項１に記載の流体サンプリング装置。
【請求項3】
前記試料ゲート手段が前記単一の部材を含み、前記単一の部材は、前記単一の部材が前記「開」位置と「閉」位置との間で移動されると前記シャフトの一つと整列する、または、ずれる路を中に含む、請求項１に記載の流体サンプリング装置。
【請求項4】
前記単一の部材は回転によって移動可能である、請求項３に記載の流体サンプリング装置。
【請求項5】
前記試料ゲート手段が前記複数の部材を含み、前記複数の部材それぞれは、前記「開」位置と「閉」位置との間で前記シャフトの一つの中で線形に移動可能な細長い部材である、請求項１に記載の流体サンプリング装置。
【請求項6】
モノリシックボディおよび細長い部材を含み、流体レセプタクルに設けられるポートに取り付けるのに好適なポート挿入部であって、
（ａ）ボディはモノリシックエラストマー材料よりなり第１の開端を第２の開端に接続するシャフトが中を通り、ボディは前記第１の開端が前記流体レセプタクルの内側に面し前記第２の開端が前記流体レセプタクルの外側に面すよう前記ポート内に略水密式に嵌合されるよう成形され、
（ｂ）細長い部材はモノリシックで剛性であり、前部および後部を含み、前記シャフト内に略水密式に嵌合されるよう成形され、前記細長い部材は前部が前記第１の開端に近接し、後部が前記第２の開端に近接した状態で前記シャフト内に嵌合され、前記細長い部材は閉位置から開位置まで前記シャフト内で移動可能であり、前記細長い部材の前記後部は可撓性管を取り付ける手段を含み、前記流体レセプタクルから前記ポート挿入部を通る流体の排出は前記細長い部材が前記閉位置を占有するとき防止され、前記細長い部材が前記開位置を占有するとき可能となる、ポート挿入部。
【請求項7】
前記細長い部材を前記開位置または前記閉位置のいずれか一方あるいはその両方で固定する一体形ロッキング手段を更に有する、請求項６に記載のポート挿入部。
【請求項8】
複数の前記細長い部材が複数の前記シャフト内で適合され嵌合される、請求項６に記載のポート挿入部。
【請求項9】
前記装置が前記ボディおよび前記細長い部材だけよりなる、請求項６に記載のポート挿入部。
【請求項10】
前記流体レセプタクルの前記ポートに取り付け可能なカラーを更に有し、前記カラーを

前記ポートに取り付けることで前記流体サンプリング装置が前記ポート内でロックされる、請求項６に記載のポート挿入部。
【請求項11】
前記カラーは前記流体サンプリング装置の一体部分である、請求項１０に記載のポート挿入部。
【請求項12】
前記流体サンプリング装置のボディは外径が０．９８５インチ（２．５ｃｍ）の円筒形であり、細長い部材は１．６００インチ（４．０６４ｃｍ）より長い長さを有する、請求項６に記載のポート挿入部。
【請求項13】
ポートが設けられる流体レセプタクルから流体の試料を無菌で抽出する流体サンプリングキットであって、
（ａ）モノリシックボディおよび細長い部材を有し、前記モノリシックボディは第１の開端を第２の開端に接続するシャフトを中に含み、前記ボディは前記第１の開端が前記流体レセプタクルの内側に面し前記第２の開端が前記流体レセプタクルの外側に面すよう前記ポート内に略水密式に嵌合されるよう成形され、前記細長い部材は前部および後部を含み、前記シャフト内に略水密式に嵌合されるよう成形され、前記細長い部材は前部が前記第１の開端に近接し、後部が前記第２の開端に近接した状態で前記シャフト内に嵌合され、前記細長い部材は開位置から閉位置まで前記シャフト内で移動可能であり、前記流体レセプタクルから前記流体サンプリング装置を通る流体の排出は前記細長い部材が前記閉位置を占有するとき防止され、前記細長い部材が前記開位置を占有するとき可能である、滅菌された流体サンプリング装置と、
（ｂ）前記細長い部材の前記後部に接続されまたは接続可能な滅菌された可撓性管と、
（ｃ）前記細長い部材が前記開位置に移動されるときに前記流体サンプリング装置を通って前記流体レセプタクルから排出される流体を収集する滅菌された収集レセプタクルであって、前記可撓性管に接続されまたは接続可能な滅菌された収集レセプタクルとを、滅菌されたパッケージ内に含んだ状態で有する、流体サンプリングキット。
【請求項14】
前記滅菌された収集レセプタクルが柔軟な袋である、請求項１３に記載の流体サンプリングキット。
【請求項15】
前記流体サンプリング装置が複数の前記シャフトと適合され嵌合される複数の前記細長い部材を有する、請求項１３に記載の流体サンプリングキット。
【請求項16】
前記流体サンプリング装置のボディは外径が０．９８５インチ（２．５ｃｍ）の円筒形であり、細長い部材は１．６００インチ（４．０６４ｃｍ）より長い長さを有する、請求項１３に記載の流体サンプリングキット。
【発明の詳細な説明】
【技術分野】
【0001】
本発明は、一般的に流体サンプリング装置に関し、特に、「一回使用の、廃棄性」に適した構造を有する一方で良好な無菌サンプリングを可能にする流体サンプリング装置に関する。
【背景技術】
【0002】
処理の進行をモニタリングするために「閉じられた」流体レセプタクル内で複雑なおよび／または注意を要する流体処理を行うとき、レセプタクルを「開ける」際に起こり得るような処理の妨げを生ずることなく流体の試料を抽出し分析することが望まれることが多い。例えば、生化学製品（例えば、生物薬剤）の研究および／または製造において、生化学的流体は無菌で「閉じられた」発酵タンク、バイオリアクタ、または同様の流体レセプタクルにしばしば含まれ、このとき流体は様々な変化する化学的且つ環境的条件下で比較

的長時間にわたって処理される。処理の過程で断続的に流体の試料を抽出し分析することで処理の進行をよりよく理解することができ、必要であれば、その結果を変えるために予防的措置がとられる。

【0003】

同様のことが、流体が導管あるいはパイプまたは他の同様の流体レセプタクルを通って導かれるときにも生ずる。この流体のサンプリングは、しばしば困難である。なぜなら、多くの工業システムにおいて、特に滅菌状態で流体の試料を抽出することを可能にするよう上記レセプタクルを簡単に開け、または、分解することができないためである。

【0004】

幾つかの流体サンプリング技法は公知であるが、ある技術的問題について述べる。例えば、ある一体化した流体サンプリング取付具は、生物薬学的用途において困難な蒸気滅菌および洗浄を使用前にしばしば必要とするステンレス鋼製のバルブおよびパイピングを有する（例えば、１９９９年９月７日にＬ．Ｄ．Ｗｉｔｔｅらに発行された米国特許第５，９４８，９９８号明細書参照）。他の流体サンプリング装置は、例えば、ホスト流体レセプタクルに特別に適合されるポートの設置を必要とすることにより既存の流体処理システムと一体化することが困難である（例えば、２０００年３月７日にＮｉｌｓ　Ａｒｔｈｕｎらに発行された米国特許第６，０３２，５４３号明細書参照）。他の装置は、標準工業ポートにおける使用に適合されるものの、全て正確に配置されるバルブ、入口、出口、シール部、針、および他の構成要素を有するが一回の滅菌周期当たり単一の無菌試料だけが可能な複雑且つ高価な機器である（例えば、１９８７年６月２日にＰｉｏ　Ｍｅｙｅｒに発行された米国特許第４，６６９，３１２号明細書参照）。最後に、上述した多くの場合のように流体サンプリング装置の大半は皮下注射器を用いて隔壁を穿孔することをそれぞれの動作において必要とする（例えば、１９８４年１月にＫ．Ｏｔｔｕｎｇに発行された米国特許第４，４２３，６４１号明細書；１９５８年７月２９日にＦ．Ｗ．Ｇｕｉｂｅｒｔに発行された米国特許第２，８４４，９６４号明細書参照）。

【図面の簡単な説明】

【0017】

【図1】流体サンプリング装置１００がポート挿入部１０、複数の可撓性導管１２０、および複数の試料用容器１３０を有する、本発明の実施形態による流体サンプリング装置１００を概略的に示す図である。

【図2】例えば、図１に示す流体サンプリング装置１００への組み込みに好適なポート挿入部１０の特定の実施形態を概略的に示す図である。

【図3A】例えば、図１に示す流体サンプリング装置への組み込みに好適なポート挿入部１０の別の特定の実施形態を概略的に示す図である。

【図3B】例えば、図１に示す流体サンプリング装置への組み込みに好適なポート挿入部１０の別の特定の実施形態を概略的に示す図である。

【図3C】例えば、図１に示す流体サンプリング装置への組み込みに好適なポート挿入部１０の別の特定の実施形態を概略的に示す図である。

【符号の説明】

【0052】

５　ホストレセプタクルのポート
１０　ポート挿入部
２０　モノリシックボディ
２２　第２の開端
２４　第１の開端
２４ａ、２４ｂ、２４ｃ、２４ｄ　シャフト開口部
２６　シャフト
３０　細長い部材
３０_{A}　前部
３０_{B}　後部

３２、３４　開口部
３６　回転式に移動可能な部材
３８　路
４０　カラー
４５　リップ部
５０　アンカー
６０　ブロック
６２　連結構造
７０　バーブ
１００　流体サンプリング装置
１２０　導管
１３０　試料用容器

【図1】

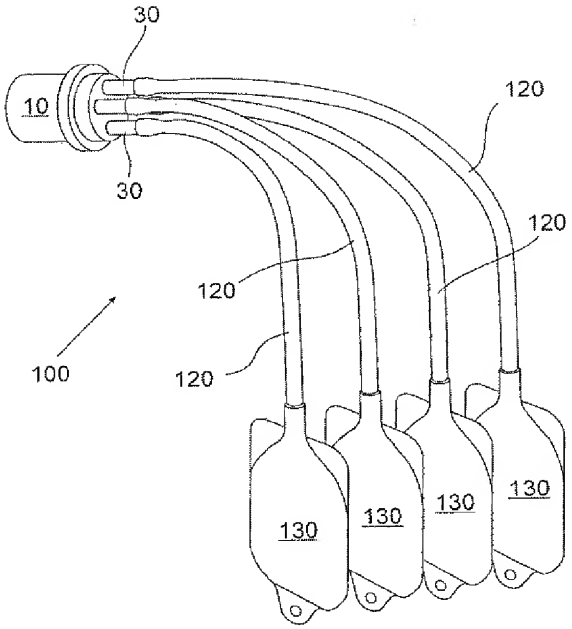

Figure 1

【図2】

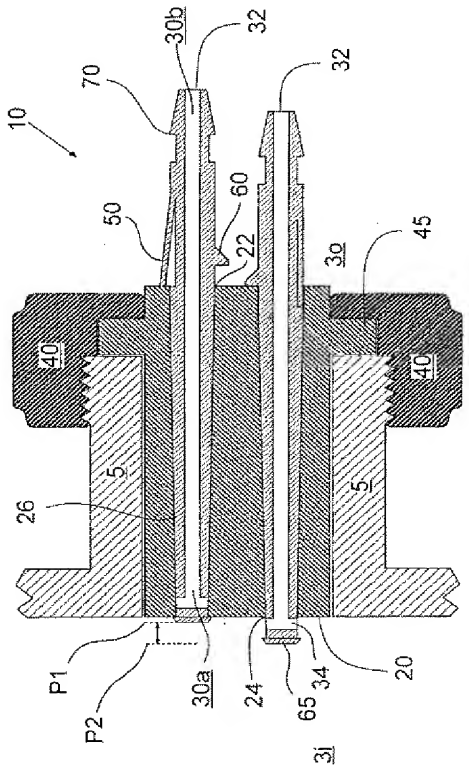

Figure 2

【図3A】

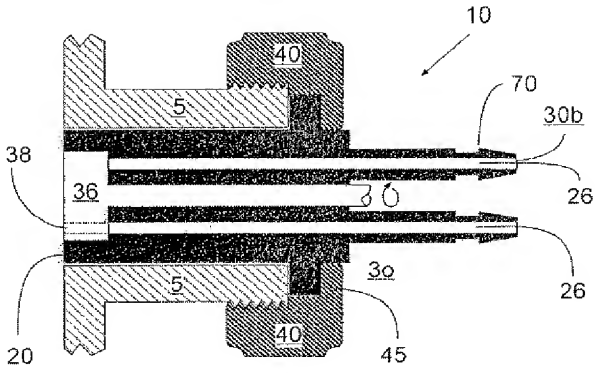

Figure 3A

【図3B】

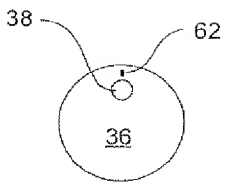

Figure 3B

【図3C】

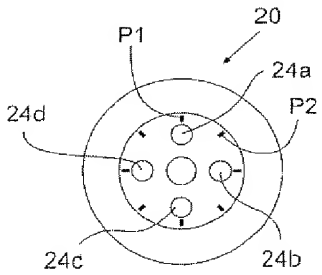

Figure 3C

【手続補正書】
【提出日】平成21年5月8日(2009.5.8)
【手続補正1】
【補正対象書類名】特許請求の範囲
【補正対象項目名】全文
【補正方法】変更
【補正の内容】
【特許請求の範囲】
【請求項1】
流体サンプルを抽出する方法であって、
（ａ）ポートを有する流体レセプタクルと、
流体サンプリング装置であって、
複数のシャフトが中を通るボディを有し、
各シャフトは前部及び後部を有し、各シャフトの前部は流体レセプタクルに向いて配置されており、シャフトの各々はシャフトの各々の長さに渡って伸びる流路へ前部で開口部を有し、
各シャフトは流体レセプタクルから装置への流体の流れを可能とする流体レセプタクルへシャフトを開けるおよび閉じる試料ゲート手段を有し、試料ゲート手段は複数の細長い部材を有し、１つの細長い部材が各シャフト内に配置され、各細長い部材は前部と後部を有し、各細長い部材の前部は流体レセプタクルに隣接して配置され、各細長い部材は、細長い部材の前部にキャップを有し、およびキャップの後方に開口部を有し、各開口部は開口部から細長い部材の後部へ各細長い部材内に形成された流路に接続され、各細長い部材は、細長い部材を通した流体レセプタクルからの流体の開放が、細長い部材が閉位置を占めるときには阻止され、細長い部材が開位置を占めるときには可能になるように、閉位置から開位置へシャフト内で線形に移動可能であり、
個々の細長い部材の後部とそれぞれ流体連通する、細長い部材の数と同じ数の複数の可撓性導管を有し、及び、
個々の導管とそれぞれ流体連通する、複数の導管と同じ数の複数の試料用容器を有する、流体サンプリング装置と、
を設けるステップと、
（ｂ）各細長い部材は閉位置にある流体サンプリング装置を流体レセプタクルのポートに取り付けるステップと、
（ｃ）流体レセプタクルを流体で充填するステップと、
（ｄ）細長い部材を選択し、所望の量の流体を試料用容器に集めるために細長い部材を閉位置から開値へ線形に移動するステップと、
（ｅ）選択された細長い部材を閉位置へ移動するステップと、
（ｆ）可撓性導管を切断し、試料用容器を分析のために取り除くステップと、
（ｇ）残りの細長い部材に対してステップ（ｄ）から（ｆ）を繰り返すステップと、
を有する流体サンプルを抽出する方法。
【請求項2】
流体サンプリング装置であって、
（ａ）複数のシャフトが中を通るボディを有し、
（ｂ）各シャフトは前部及び後部を有し、各シャフトの前部は流体レセプタクルに向いて配置されており、シャフトの各々はシャフトの各々の長さに渡って伸びる流路へ前部で開口部を有し、
（ｃ）各シャフトは流体レセプタクルから装置への流体の流れを可能とする流体レセプタクルへシャフトを開けるおよび閉じる試料ゲート手段を有し、試料ゲート手段は複数の細長い部材を有し、１つの細長い部材が各シャフト内に配置され、各細長い部材は前部と後部を有し、各細長い部材の前部は流体レセプタクルに隣接して配置され、各細長い部材は、細長い部材の前部にキャップを有し、およびキャップの後方に開口部を有し、各開口部

は開口部から細長い部材の後部へ各細長い部材内に形成された流路に接続され、各細長い部材は、開位置にあるときには流体が流体レセプタクルからキャップを通り開口部へ流れることができるが閉位置にあるときには流れることができないように、閉位置と開位置の間で線形に移動可能であり、

（ｄ）個々の細長い部材の後部とそれぞれ流体連通する、細長い部材の数と同じ数の複数の可撓性導管を有し、及び、

（ｅ）個々の導管とそれぞれ流体連通する、複数の導管と同じ数の複数の試料用容器を有する、流体サンプリング装置。

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【外国語明細書】

Specification
Title of Invention
DISPOSABLE, PRE-STERILIZED FLUID RECEPTACLE SAMPLING DEVICE

Field

In general, the present invention is directed to a fluid sampling device, and in particular, to a fluid sampling device having a configuration amenable to "single-use disposability", while still enabling good aseptic sampling.

Background

When conducting complex and/or delicate fluid processes within a "closed" fluid receptacle, to monitor the progress of the process, it is often desirable to withdraw and analyze samples of the fluid without disturbing the process, such as may occur upon "opening" the receptacle. For example, in the study and/or manufacture of biochemical products (*e.g.*, biopharmaceuticals), biochemical fluid is often contained in an aseptically "closed" fermenting tank, bioreactor, or like fluid receptacle, wherein the fluid is processed over comparatively long periods of time, under diverse and changing chemical and environmental conditions. By withdrawing and analyzing samples of the fluid intermittently in the course of the process, one can learn more about the progress of the process, and if called for, take prophylactic measures to change the outcome thereof.

Similar issues arise also in instances wherein fluid is conducted through a conduit, or a pipe, or other like fluid receptacle. Sampling of said fluid is often difficult because in many industrial systems, said receptacles are not easily opened or disassembled to allow one to withdraw fluid samples, especially in a sterile manner.

While several fluid sampling techniques are known, certain technical issues can be noted. For example, certain integrated fluid sampling fixtures comprise stainless steel valves and piping which, for biopharmaceutical applications, often require laborious steam sterilization and cleaning prior to use. (*See e.g.*, U.S. Pat. No. 5,948,998, issued to L.D. Witte et al. on September 7, 1999). Other fluid sampling devices are difficult to integrate into extant fluid processing systems, for example, by requiring the installation of custom-fitted ports onto a host fluid receptacle. (*See e.g.*,

U.S. Pat. No. 6,032,543, issued to Nils Arthun *et al.* on March 7, 2000). Still other devices, although adapted for use in standard industrial ports, are complex and costly instruments comprising valves, inlets, outlets, seals, needles, and other components, all precisely arranged, but capable of only a single aseptic sample per sterilization cycle. (*See e.g.*, U.S. Pat. No. 4,669,312, issued to Pio Meyer on June 2, 1987). Finally, the majority of fluid sampling devices -- as is the case in many of those already mentioned -- require in their operation the piercing of a septum using a hypodermic needle. (*See also, e.g.*, U.S. Pat. No. 4,423,641, issued to K. Ottung on January 1984; and U.S. Pat. No. 2,844,964, issued to F.W. Guibert on July 29, 1958).

In light of the above, a need exists for a fluid sampling device that is sufficiently inexpensive in its construction to promote single-use disposability, capable of being used in standard industrial ports commonly found in fluid receptacles, and capable of several good sterile fluid sample withdrawals per sterilization cycle and/or prior to being exhausted.

Summary

The present invention provides a fluid sampling device comprising a port insert, a plurality of flexible conduits, and a plurality of sample containers. The port insert comprises a body having a plurality of shafts therethrough, and sample grating means for individually opening and closing any of said shafts to control the flow of fluid therethrough. The sample gating means comprise single or multiple members that are displaceable between "open" and "closed" positions such that fluid can flow through said body through one of said shafts in said "open" position, but not in said "closed" position. Each shaft is in fluid communication with a flexible conduit, which in turn, is in fluid communication with a sample container. The sample containers are preferably flexible bags; and the conduits, preferably, flexible tubing.

In a principal embodiment, the port insert is configured as a monolithic body having a plurality of rigid elongate members disposed therethrough in a manner allowing linear displacement of said members between said "closed" and "open" positions. When the port insert is installed into a suitable port provided on a fluid receptacle, an elongate member can be moved into its "open" position, whereupon, fluid contained within the receptacle flows into the elongate member, then through the flexible conduit, and ultimately into the sample container. After the desired amount of fluid is collected in the sample container, the elongate member is moved and locked into its "closed" position, the flexible conduit is severed (preferably, aseptically), and the sample container taken for further analysis. The process can then be repeated, by using the remaining elongate members. When all elongate members are exhausted,

the port insert is fully spent and can be easily removed and replaced after the fluid processes in the fluid receptacle are concluded.

In light of the above, it is a principal object of the present invention to provide a fluid sampling device.

It is another object of the present invention to provide a fluid sampling device that enables the withdrawal of several samples of fluid from a fluid receptacle.

It is another object of the present invention to provide a fluid sampling device that enables the withdrawal of several samples of fluids from a fluid receptacle, wherein said withdrawal occurs in a substantially sterile manner, and wherein inter-sample cross-contamination is substantially discouraged.

It is another object of the present invention to provide a fluid sampling device that enables the withdrawal of several samples of fluid from a fluid receptacle, the fluid sampling device capable of being configured to promote so-called "single-use disposability".

It is another object of the present invention to provide a fluid sampling device comprising a port insert, a plurality of flexible conduits, and a plurality of sample containers (preferably, flexible, bag-like sample containers).

It is another object of the present invention to provide a port insert useful for making a fluid sampling devices, said port insert maximizing functionality with a minimal number of comparatively inexpensive components, thus promoting said "single use disposability".

It is another object of the present invention to provide a kit containing in sterilized packaging the assembled, partially assembled, or unassembled components of a fluid sampling device, wherein all contained components are sterilized.

These and other objects of the present invention can be better understood in view of the detailed description herein, read in conjunction with the attached drawings.

Brief Description of the Drawings

Figure 1 schematically illustrates a fluid sampling device 100 according to an embodiment of the present invention, the fluid sampling device 100 comprising a port insert 10, a plurality of flexible conduits 120, and a plurality of sample containers 130.

Figure 2 schematically illustrates a particular embodiment of a port insert 10 suitable for incorporation, for example, into the fluid sampling device 100 shown in Figure 1.

Figures 3, 3A, and 3B schematically illustrate another particular embodiment of a port insert 10 suitable for incorporation, for example, into the fluid sampling device shown in Figure 1.

Detailed Description

As illustrated in Figure 1, the fluid sampling device 100 of the present invention comprises, in general, a port insert 10, a plurality of flexible conduits 120, and a plurality of sample containers 130. When the port insert 10 is "plugged" into a host fluid receptacle (such as a bioreactor vessel or pipe), samples of fluid can be removed sequentially from the host fluid receptacle, and collected in individual sample containers, without substantially disturbing, corrupting, or otherwise affecting any ongoing fluid processes occurring within the host. Upon completion of said fluid processes, the spent (or partially spent) fluid sampling device 100 is removed, allowing comparatively easy replacement with a fresh unit prior to conducting another of said fluid processes.

The port insert 10 includes a plurality of shafts, each providing an avenue through which fluid can flow from the host fluid receptacle into one of said sample container 130. The port insert 10 further comprises sample gating means for individually opening and closing said shafts to control the flow of fluid therethrough. The sample gating means comprise single or multiple members displaceable between "open" and "closed" positions such that fluid can flow through said body through one of said shafts in said "open" position, but not in said "closed" position. Each individual elongate member is connected to (or otherwise in fluid communication with) a flexible conduit, which in turn, is connected to (or otherwise in fluid communication with) a sample container.

In operation, prior to being charged with fluid, a host fluid receptacle is cleaned, sterilized, and otherwise prepared for processing. The pre-sterilized fluid sampling device is installed into an existing port provided in the host and steam "sterilized-in-place". The fluid receptacle is then charged with the fluid, and fluid processing commences.

During the processing of the fluid, when a sample is desired for analysis, the sample gating means is displaced into an "open" position, whereupon fluid flows out of the host receptacle, through the active shaft, then through the attached fluid conduit, and ultimately into the sample container. After the desired quantity of fluid is collected, sample gating means is displaced into a "closed" position. The flexible conduit is then clamped off at two points, then severed between the two clamps, so that the captured sample can be removed for analysis. Preferably, a heat knife, flame, or the like, is used to both sever and seal the conduit simultaneously.

As the fluid process continues, if further samples are desired, another of the remaining unused shaft can be activated. This continues until all shafts are spent, or the fluid process ends. At the end of the fluid process, the fluid sampling device is removed, and disposed off in accordance with appropriate industrial practice. When the host receptacle is again needed for another processing operation, a fresh fluid sampling device is installed.

The fluid sampling device 100 is preferably made as a "single use" item. In this regard, it is "single use" in the sense that at the completion of the desired (or predetermined) number of fluid sampling operations, the device 100 can either be disposed (*e.g.*, as is sometimes required by law after sampling certain environmentally-regulated substances) or partially recycled (*e.g.*, after dispensing non-regulated substances).

Although subject to several and diverse configuration, a preferred embodiment of the port insert is shown in Figure 2. The port insert 10 therein comprises a monolithic body 20 and a plurality of elongate members 30. The body 20 -- preferably made of a monolithic elastomeric material -- is provided with shafts 26 therethrough connecting first open ends 24 with a second open ends 22. The body is shaped to fit substantially water-tight within the host receptacle's port 5 -- much like a cork or plug or stopper -- and such that the first open ends 24 are facing inside the fluid receptacle 3_i, with the second open ends 22 facing outside the fluid receptacle 3_o.

In respect of materials and methods, the body 20 of the port insert 10 will generally be formed monolithically (*i.e.*, as a single, homogenous, unitary, unassembled piece) from polymeric material, for example, by well-known injection molding or like processes.

Examples of suitable polymeric material include, but are not limited to, polycarbonates, polyesters, nylons, PTFE resins and other fluoropolymers, acrylic and methacrylic resins and copolymers, polysulphones, polyethersulphones, polyaryl-sulphones, polystryenes, polyvinyl chlorides, chlorinated polyvinyl chlorides, ABS and its alloys and blends, polyurethanes, thermoset polymers, polyolefins (*e.g.*, low density polyethylene, high density polyethylene, and ultrahigh molecular weight polyethylene and copolymers thereof), polypropylene and copolymers thereof, and metallocene generated polyolefins.

The body 20 should be formed in consideration of conditions likely to be encountered in the course of *in situ* steam sterilization. The temperature and pressure of such sterilization is typically about 121°C and 1 bar above atmospheric pressure. The use of temperatures and pressures up to and in excess of 142°C and 3 bars is not too uncommon.

To accommodate easy installation of the fluid sampling device into the host receptacles, the port insert should be substantially cylindrical in shape and have an external diameter of about .985 inch (2.5 cm.) In the biopharmaceutical field, such configuration will allow the fluid sampling device 10 to be installed, without further custom engineering, into several commercially-available types of bioreactors, that already contain ports (*e.g.*, so-called "Ingold Ports") of such dimensions, and which are currently used for probes and other sensors.

Each of the elongate members 30 are monolithic and rigid, and has a front 30_A and a back 30_B. They are shaped to fit substantially water-tight within said shaft 26 such that the front thereof 30_A is proximate the first open end 24 and the back thereof 30_B is proximate the second open end 22. Each elongate member 30 is movable within said shaft 26 from a closed position P_1 to an open position P_2, such that the release of fluid out of said fluid receptacle through said port insert 10 is frustrated when the elongate member 30 occupies the closed position P_1 and enabled when the elongate member 30 occupies the open position P_2.

In a desirable embodiment, four elongate members, each having a length equal to or slightly greater than 1.600 inch (4.064 cm), are provided on the port insert 10. As shown in Figure 2, each elongate member 30 is preferably configured as a hollow tube with a fluid passage way running substantially the entire length front 30_A to back 30_B, culminating in openings 34 and 32 on both ends of the member. The opening(s) 34 on the front end 30_A are "uncovered" or otherwise made accessible to fluid only when the elongate member is moved into its "open" position P_2.

Although port insert 10 is structured to fit snugly within host port, to prevent it from being popped into or out of the port during use, additional mechanical restraints are highly desirable. As shown in Fig. 2, this is accomplished by means of a threaded collar 40 that engages with and holds an annular lip 45 provided on the port insert when said collar 40 is screwed into port 5. Other mechanical restraints -- such as clamps, screws, bolts, or mated interlocking parts -- are known in the art. The mechanical restraints are preferably temporary mechanical devices that allow easy removal and disposal of spent devices.

As an alternative to a sample gating means comprising multiple elongate members, the present invention also contemplates a port insert comprising a single displaceable member that, by itself, functions to selectively and individually "open" and "close" each shaft provided in the port insert. A representative example of such sample gating means is presented in Figure 3.

In Figure 3, the alternative port 10 comprises (a) a body 20 having a plurality of shafts 26 therethrough and (b) a rotatably displaceable member 36. Rotatably displaceable member 36 is provided with a passage 38 which can be

selectively rotated into alignment with any of the shaft openings 24a, 24b, 24c, and 24d disposed on body 20. When the passage 38 and an opening are aligned, fluid sample can flow through the port insert 10 through the respectively selected shaft.

In practice -- in contrast to the schematic nature of Fig. 3 -- both the passage 38 and member 36 should be structurally configured to optimize fluid flow, for example, by streamlining these parts to minimize so-called "dead spaces". Such configurations will vary among different applications. Regardless, suitable flow optimizing strategies are well known in the art.

The rotatably displaceable member 36 can be rotated by means of an integrated handle (partially shown in Figure 3) that extends through and past the body 20. Where appropriate, the handle should extend sufficiently far from the body 20 to provide sufficient clearance for conduits to be connected to barbs 70, and thereby discourage potential restriction to flow resultant of pinching and/or extreme bending of the conduits.

As an alternative to an integrated handle, one can also employ a separate tool (*e.g.*, an allen wrench or screwdriver) to turn the rotatably displaceable member 36. For such instance, the rotatably displaceable member is configured with an appropriate tool engaging structure (*e.g.*, slots, nuts, bolts, *etc.*).

Preferably, the rotatably displaceable member 36 should be capable of rotation in a single direction only, *i.e.*, either clockwise or counter-clockwise, and such that alignment in any of the achievable "closed" or "open" positions, respective of said shafts, are definitively and discretely defined. Means should also be provided to prevent the member 36 from being rotated back into alignment with any spent shafts.

As shown schematically, in Figures 3A and 3B, discrete positions can be defined by using corresponding interlocking structures 62 and P1/P2 provided respectively on rotatably displaceable member 36 and monolithic body 20. When structure 62 (*e.g.*, a tab) is engaged with structure P1 (*e.g.*, a slot), passage 38 is aligned definitively with opening 24a. Thus, the shaft 26 corresponding to opening 24a is "open" and "active", and the shafts corresponding to openings 24b, 24c, and 24d are "closed" and "inactive". After the desired volume of sample fluid has flown through the "active" shaft, it is then closed by rotating the member 36 such that structure 62 engages with structure P2 (*e.g.*, another slot). In this position, passage 38 is not aligned with any of openings 24a, 24b, 24c, and 24d, and thus, all shafts correspondent therewith are "closed" and "inactive". When desired, the remaining unused shafts can be "opened" and "closed" sequentially in the same manner. Those skilled in the art will know of suitable configurations (*e.g.*, a ratchet-like configuration) that can render member 26 rotatable in one direction only, as well as prevent it from being rotated more than one time around (*e.g.*, a brake or other physical obstruction).

To further assist manual rotation and alignment, graphical, textual, or otherwise informative indicia or structures (*e.g.*, a pointer in combination with symbolic icons) can be integrated into or otherwise provided on, for example, the handle, the body 20, or both, to inform a user of the current position of rotatably displaceable member 26. Likewise, the interlocking structures (*e.g.*, 38, P1, and P2) can also be configured to provide an audible (*e.g.*, clicking) or frictional (*e.g.*, variable resistance) clue to a user during rotation indicative of the displacement and/or position of the rotatably displaceable member 36.

As mentioned, the sample containers used for the present invention are preferably flexible bags, particularly so when the fluid sampling device is intended for use in biopharmaceutical applications or like applications that have comparatively high aseptic requirements. Unlike many conventional sampling devices, the fluid sampling device 100 of the present invention does not rely on valves, pumps, and like extrinsic mechanisms to promote, urge, facilitate, or otherwise affect the flow of sample liquid out of the host fluid receptacle 5 into an available sample container 130. Rather, fluid flows through the aseptically-isolated flow path of the device 100 by a combination of ambient gravitational forces and the extant pressurization of the host fluid receptacle. Initially provided in a collapsed or partially-collapsed state, the flexible bag (or functionally-equivalent expansible fluid container) expands, decompresses, or otherwise "fills-out" as withdrawn sample fluid flows thereinto.

Although the use of a flexible, bag-like sample container 130 is preferred, a rigid sample container can also be used without departing from objectives of the present invention. For example, the sample container can be configured as a spacious, rigid box, bulb, vial, or bottle. A vent -- preferably of modest construction -- can be provided to permit the displacement of contained gas as sample fluid flows thereinto.

One type of vent (not shown) that can be implemented with little cost, yet still provide good aseptic functionality, is constructed by "patching" and opening the rigid container (*i.e.*, above the expected fluid fill level thereof) with a gas permeable sheet of fluoropolymer membrane (e.g., "Gore-Tex"-brand membrane available from W.L. Gore and Associates of Wilmington, Delaware) or a substantially gas permeable sheet of polyethylene fiber (e.g., "Tyvek"-brand material available from E.I. du Pont de Nemours, Inc. of Wilmington, Delaware).

As an alternative to complete rigidity, it is envisioned that a sample container comprise rigid side walls that bend and flex along folds or creases or crumple zones, and the like, such that the sample container is capable of collapsing or otherwise diminishing its volume. Examples of collapsible rigid configurations include

accordion-like configurations, bellows-like configurations, and other configurations having pleated side walls.

The mechanisms underlying the operation of the fluid sampling device 100 call for a certain rigidity in the configuration of elongate members 30. Aside from durability, the rigidity allows the members to be pushed through the shaft into their open positions with sufficient and appropriate force to overcome the frictional forces that create the liquid tight seal, without the elongate member flexing, bending, crumpling, or otherwise deforming, such circumstances potentially leading to sampling failures, and/or more catastrophically, breach of extant sterile conditions.

Because several rigid members 30 are provided through the port insert 30, physical space immediately outside the insert will likely be cramped, and may not accommodate sample containers large enough to collect the volumes of fluid desired. Hence, the sample containers are placed further geographically downstream of the elongate members 130, with lengths of flexible conduit material 120 provided therebetween.

Although a flexible conduit and a flexible bag-like sample container can be formed as one component, in all likelihood, the conduits 120 and elongate members 30 -- owing to their differing preferred material composition -- are formed separately and later assembled. For example, in one embodiment, conduits 120 are made of flexible elastomeric material, whereas elongate members 30 are made of high-impact, rigid polymeric material. In such and like instances, the back end 30_B of each rigid elongate member 30 can be provided with means for securely attaching the flexible conduit, such as the barbed end 70 shown in Figure 2.

In the preferred configuration, means should be provided to prevent the elongate means from being prematurely moved into its open position, as well as prevent it from being moved too far past its open and/or closed positions. While such means will vary depending on the ultimate configuration of the fluid sampling device, the embodiment represented in Figure 2 illustrates certain examples thereof. For example, anchor 50 is provided to prevent the elongate member 30 from being pushed into its open position P_2 prematurely. When sampling is commenced, the anchor 50 can be moved into a position in which it no longer impedes the transit of the member 30 through the shaft. When pushed in, block 60 prevents the member from being pushed in too far. A cap 24 can also be provided on the front 30_A of member 30 to -- in addition to creating a liquid tight seal -- prevent the member 30 from being pulled out.

For applications having comparatively strict sterility requirements (*e.g.*, biopharmaceutical applications), the present invention is preferably embodied in kit form, comprising, enclosed within sterile packaging, the following principal kit contents: (a) a pre-sterilized port insert constructed in accordance with any embodiment

described and/or otherwise enabled herein; (b) a supply of pre-sterilized flexible tubing, preferably "pre-cut to length", connected or connectable to the elongate members of said port insert; and (c) a supply of pre-sterilized sample containers connected or connectable to said flexible tubing, the pre-sterilized sample containers also constructed in accordance with any embodiment described and/or otherwise enabled herein. It is preferred that the kit be pre-assembled and then sterilized in its bag or container, using well known means such as gamma radiation, ethylene oxide gas, and the like.

The provision of the present invention in kit form advances certain objectives either not possible or difficult to accomplish otherwise. Foremost, the kit assures that all its contents are pre-sterilized, and essentially remain so until use. Further, ease of installation, assembly, and operation are improved since all kit contents are pre-selected, pre-sized, and pre-matched to assure proper fit and assembly. And, along similar lines, a kit-based approach promotes standardization of the kit's contents, as well as their manufacture and packaging, leading to reduced product costs, fostering the product's "disposability", and broadening the accessibility of the technology to the public.

Optionally, the kit may also contain, for example, means for locking the port insert within the port provided on a host fluid receptacle (*e.g.*, collar 40); accessories and other means used for assembling the fluid sampling device (*e.g.*, clamps, connectors, junctions, manifolds, and the like); means for mounting, fixing, and/or positioning the assembled fluid sampling device relative to the host receptacle (*e.g.*, adhesive strips, fasteners, brackets, and the like); and a disposal bag for disposing a spent fluid sampling device. These and other optional kit contents, if included, are all sterilized in their packaging. Both the principal and optional kit contents can be provided, if desired, individually or collectively wrapped (*i.e.*, in groups) within said sterile packaging, thus providing additional sterile barriers.

Although certain embodiments of the invention are disclosed, those skilled in the art, having the benefit of the teaching of the present invention set forth herein, can affect numerous modifications thereto. These modifications are to be construed as encompassed within the scope of the present invention as set forth in the appended claims.

Claims

1. A fluid sampling device comprising:

(a) a port insert comprising a body having a plurality of shafts therethrough, and sample gating means for individually opening and closing any of said shafts to enable the flow of fluid, said sample gating means comprising single or multiple members displaceable between "open" and "closed" positions such that fluid can flow through said body through one of said shafts in said "open" position, but not in said "closed" position;

(b) a plurality of flexible conduits, equal in number to said plurality of shafts, each flexible conduit in fluid communication with an individual shaft; and

(c) a plurality of sample containers, equal in number to said plurality of conduits, each sample container in fluid communication with an individual conduit.

2. The fluid sampling device of claim 1, wherein said sample containers are flexible bags.

3. The fluid sampling device of claim 1, wherein said sample gating means comprises said single member, said single member having a passage therethrough that can be brought into and out of alignment with one of said shafts when said single member is displaced between said "open" and "closed" positions.

4. The fluid sampling device of claim 3, wherein said single member is displaceable by rotation.

5. The fluid sampling device of claim 1, wherein said sample gating means comprises said multiple members, each of said multiple members being an elongate member linearly displaceable within one of said shafts between said "open" and "closed" positions.

6. A port insert suitable for installation into a port provided in a fluid receptacle, said port insert comprising a monolithic body and an elongate member, wherein:

(a) the body is a monolithic elastomeric material with a shaft therethrough connecting a first open end with a second open end, the body being shaped to fit substantially water-tight within said port such that said first open end faces inside said fluid receptacle and said second open end faces outside said fluid receptacle; and

(b) the elongate member is monolithic and rigid, has a front and a back, and is shaped to fit substantially water-tight within said shaft, said elongate member being fitted within said shaft with the front thereof proximate said first open end and the back thereof proximate said second open end, said elongate member being movable within said shaft from a closed position to an open position, said back of said elongate member having means for attaching a flexible tube, the release of fluid out of said fluid receptacle through said port insert being preventable when said elongate member occupies said closed position and allowable when said elongate member occupies said open position.

7. The port insert of claim 6, further comprising integral locking means to secure said elongate member in either said open position or said closed position or both.

8. The port insert of claim 6, having a plurality of said elongate members matched and fitted within a plurality of said shafts.

9. The port insert of claim 6, wherein said device consists only of said body and said elongate member.

10. The port insert of claim 6, further comprising a collar attachable to said port on said fluid receptacle, whereby said fluid sampling device can be locked within said port by attaching said collar to said port.

11. The port insert of claim 10, wherein said collar is an integral part of said fluid sampling device.

12. The port insert of claim 6, wherein the body of said fluid sampling device is cylindrical in shape having a external diameter of .985 inch (2.5 cm.); and the elongate member has a length greater than 1.600 inch (4.064 cm).

13. A fluid sampling kit for aseptically retrieving a fluid sample from a fluid receptacle, the fluid receptacle provided with a port, the fluid sampling kit comprising, enclosed within sterilized packaging, the following:

(a) a sterilized fluid sampling device comprising a monolithic body and an elongate member, said monolithic body having a shaft therethrough connecting a first open end with a second open end, said body shaped to fit substantially water-tight within said port such that said first open end faces inside said fluid receptacle and said

second open end faces outside said fluid receptacle, said elongate member having a front and a back and shaped to fit substantially water-tight within said shaft, said elongate member being fitted within said shaft with the front thereof proximate said first open end and the back thereof proximate said second open end, said elongate member being movable within said shaft from an open position to a closed position, whereby the release of fluid out of said fluid receptacle through said fluid sampling device is prevented when said elongate member occupies said closed position and allowed when said elongate member occupies said open position;

(b) a sterilized flexible tube connected or connectable to said back of said elongate member; and

(c) a sterilized collection receptacle for collecting fluid released from said fluid receptacle through said fluid sampling device when said elongate member is moved to said open position, the sterilized collection receptacle being connected or connectable to said flexible tube.

14. The fluid sampling kit of claim **13**, wherein said sterilized collection receptacle is a flexible bag.

15. The fluid sampling kit of claim **13**, wherein said fluid sampling device has a plurality of said elongate members matched and fitted within a plurality of said shafts.

16. The fluid sampling kit of claim **13**, wherein the body of said fluid sampling device is cylindrical in shape having a external diameter of .985 inch (2.5 cm.) and the elongate member has a length greater than 1.600 inch (4.064 cm).

1. Abstract

The present invention provides a fluid sampling device comprising a port insert, a plurality of flexible conduits, and a plurality of sample containers. The port insert comprises a body having a plurality of shafts therethrough and sample gating means for individually opening and closing any of said shafts to enable the flow of fluid therethrough. The flexible conduits (*e.g.*, flexible tubing) are equal in number to the elongate member, with each flexible conduit connected to or otherwise in fluid communication with an individual shaft. Similarly, the sample containers (*e.g.*, flexible bags) are equal in number to the conduits, with each sample container connected to an individual conduit opposite the connection to the shaft. A specific configuration for the port insert, as well as kit containing sterilized components of the fluid sampling device, are also described.

2. Representative Drawing

Fig. 1

Fig. 1 【図3C】

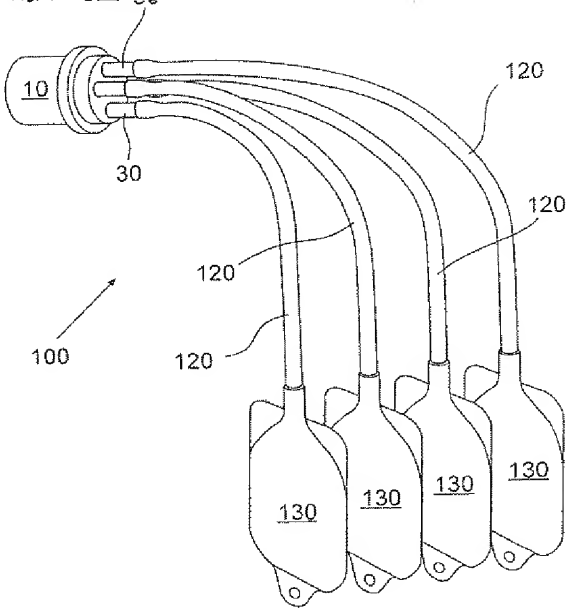

Figure 1

Fig. 2

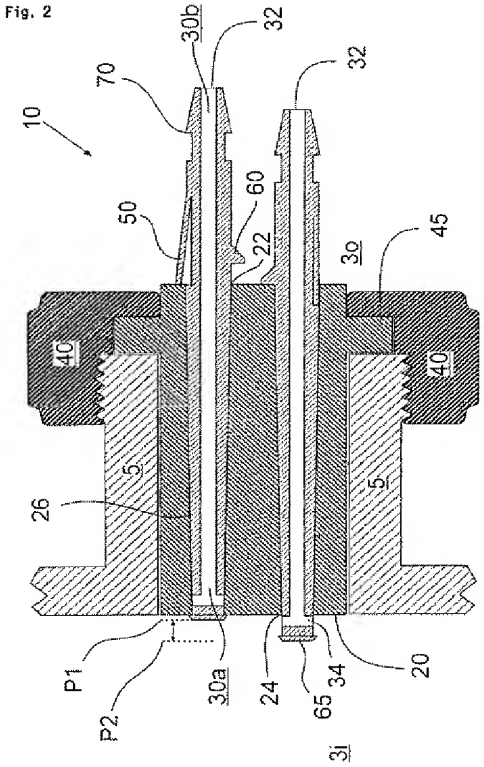

Figure 2

Fig. 3

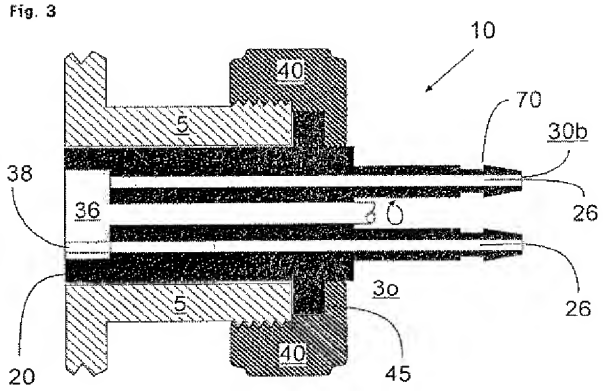

Figure 3

Fig. 3 A

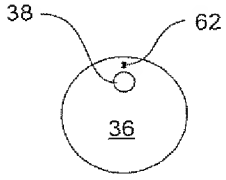

Figure 3A

Fig. 3 B

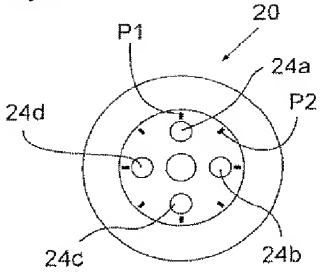

Figure 3B